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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/884,183	06/19/2001	Bret S. Weinstein	45421/RAS/W397	2814

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EXAMINER	
PARAS JR, PETER	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/884,183	WEINSTEIN, BRET S.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-7* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *0702* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group III, claims 5-7, in Paper No. 0903 is acknowledged.

Claims 1-4 and 8-20 have been cancelled. Claims 5-7 are pending and are under current consideration.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5-7 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to methods of breeding an animal line for experimental use, comprising selecting a first population of animals that comprise telomeres of determinable lengths, determining a statistical distribution of telomere lengths and permitting animals with a desired distribution of telomere lengths to produce offspring. The claims are further directed to altering a telomere length of one or more chromosomes contained within a germ cell of an animal of the first population.

The instant specification has contemplated that introduction of a desirable distribution of telomere lengths in a breeding population of animals will produce a model animals better suited for testing agents. The instant specification has further contemplated that telomere length can be adjusted enzymatically or as a result of nuclear transfer. The instant specification has purported that a fixed optimum target for telomere length can be set in order to produce model organisms better suited to illuminate dangers of one of two opposing types carcinogenic effects and tissue damage/accelerated aging. The instant specification has asserted that testing agents on two populations will provide better total resolution than testing agents on a single population.

The instant specification has disclosed methods of breeding animals to produce populations having a desired length of telomeres. The claims embrace such methods. The instant specification has discussed that optimization of telomere lengths could allow for more accurate testing of agents with respect to carcinogenicity and accelerated aging. However, the evidence of record does not provide a correlation between optimization of telomere lengths and any disease or disorder. The specification has provided general assertions that the claimed methods may be used to more accurately test agents.

As such, the asserted utility, for the claims methods as provided by the instant specification and encompassed by the claims, does not appear to be specific and substantial. The asserted utility does not appear specific and substantial to the skilled artisan since the evidence of record has not provided any suggestion of a correlation

between telomere length and any disease or disorder. Since the evidence of record has not provided a correlation between telomere lengths and any disease or disorder, the utility of optimizing telomere length in a population of animals is not apparent. The evidence of record has not provided any other utilities for the methods embraced by the claims that are specific, substantial, and credible.

The asserted utility of the methods embraced by the claims is based on the expectation that optimizing telomere length would provide better conditions for testing agents. While the telomere lengths are known to vary as a result of nuclear transfer, the association of telomere length with any disease has yet to be elucidated. In fact the art suggests that telomere lengths in cloned cattle vary according to the cell type used. See Miyashita (Biology of Reproduction, 2002, 66: 1649-1655). Miyashita report that telomeres of cloned calves derived from epithelial cells were surprisingly shorter than those in control cattle. Furthermore, Miyashita suggest that differences in telomere length between species of cloned mammals might be due to species differences, differences in nuclear transfer techniques or donor cell types.

Therefore, the art suggests a need to provide independent evidence of an association of telomere length with a disease or disorder. However, neither the specification nor any art of record provides evidence of the existence of a correlation between telomere length and a disease or disorder, leaving the skilled artisan to speculate and investigate the uses of the optimization of telomere length in a population of animals as embraced by the claimed methods. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for

the claimed methods. In light of the above, the skilled artisan would not find the asserted utility of the claimed invention to be specific and substantial.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In the addition the following issues under enablement should be considered:

The specification has contemplated that nuclear transfer could be used to alter telomere length. The art of nuclear transfer however is unpredictable art. The state of the art clearly indicates that the nuclear transfer technique itself is responsible for the abnormal phenotypes of cloned animals. Cross et al (2001, PNAS Vol. 98, No. 11, pages 5949-5951) suggests that cloning has many complications such as fetal and placental overgrowth. Cross goes on to report that "animals also frequently suffer from

congenital anomalies and dies with in hours of birth. Embryonic and fetal losses are also extremely high, such that far less than 1% of manipulated embryos give rise to live-animals. These grim facts, collectively termed here cloned offspring syndrome, have raised considerable concern about the cloning process. The reasons for these complications have raised considerable concern for the cloning process." See Cross, on page 5949, in column 1. Eggan et al support such observations by reporting a serious impediment to the general utility of the procedure [transfer of embryonic and somatic nuclei into enucleated oocytes] is the low survival rate of cloned animals. See page 6209 in column 1. Eggan goes on to report that the defects of cloned animals, in species including sheep, cows, and mice, are not limited to only extra-embryonic cells, but that in addition to placental abnormalities also include fetal overgrowth and respiratory failure. Such abnormalities are often associated with neonatal mortality. The factors that contribute to these abnormalities as well as the parameters that affect the long-term survival of clones remain undefined. See Eggan on page 6209, column 1. Moreover, Eggan et al has directly correlated abnormalities, such as fetal overgrowth, to nuclear transfer techniques in studies that compare development of reconstructed mouse embryos with the development of mouse embryos created from ES cell complementation of a tetraploid blastocyst. See page 6210, column 1; page 6212, column 2; figure 4 on page 6213; and page 6214, column1. Other abnormalities, such as respiratory failure, are suggested to be a direct consequence of the genetic makeup of the donor cell nucleus and not the result of nuclear transfer techniques (see Eggan on pages 6213-6214); such observations add another level of complexity and

unpredictability to creating cloned non-human mammals. Also see Wilmut et al and Baguisi et al who report on the unpredictability of cloning sheep and goats respectively. Given the unpredictable state of the nuclear transfer art it would have required undue experimentation to make and use the invention as claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time). The examiner is scheduled to move a new office, on 1/13/2004, having a new telephone number as follows: 571-272-0732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER